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SEIZURE DISORDERS

ABSENCE EPY OUTCOME AND RESPONSE TO INITIAL THERAPY

The prognostic significance of initial antiepileptic drug (AED) failure in children with absence epilepsy was studied at the IWK-Grace Health Center, Dalhousie University, Halifax, Nova Scotia, Canada. Patients were identified by review of centralized EEG records, and follow-up was conducted by parent mail-in questionnaire or physician review of records. Of 86 patients followed for >24 months (median 171 months), 52 (60%) responded to the initial AED with complete seizure control for >1 year before final follow-up. Of 22 initially treated with valproate (VPA), 17 (77%) responded compared with 35 (55%) of 64 treated with either ethosuximide (32 of 59) or clonazepam (3 of 5) (p=0.07). Final remission rate was 69% when the initial AED was successful compared to 41% when it failed (p<0.02). Other seizure types (generalized tonic-clonic or myoclonic) coexisting before or during initial AED treatment were risk factors for a lower response rate. Patients whose initial treatment failed were more likely to develop juvenile myoclonic epilepsy (32% cf 10%; p<0.02) and intractable epilepsy (17% cf 2%; p<0.04). (Wirrell E, Camfield C, Camfield P, Dooley J. Prognostic significance of failure of the initial antiepileptic drug in children with absence epilepsy. Epilepsia June 2001;42:760-763). (Reprints: Dr Elaine Wirrell, Department of Pediatrics, Division of Neurology, Alberta Children's Hospital, 1820 Richmond Rd, SW, Calgary, AB, Canada T2T 5C7).

COMMENT. The initial AED treatment of absence epilepsy is successful in 60% of children. Ethosuximide is favored as the initial treatment of choice but the response rate to valproate is greater. Risk factors for a lower final remission rate include failure of the initial AED and coexisting generalized tonic-clonic or myoclonic seizures. Poor response to the initial therapy is also predictive of progression to juvenile myoclonic or intractable epilepsy.

Similar conclusions were reported following a meta-analysis study of 2303 patients from 26 publications of 23 cohorts conducted at Leiden University Hospital, The Netherlands (Bouma PAD et al, 1996; see Progress in Pediatric Neurology III, PNB Publishers, 1997;pp60-62). The poorest outcomes occurred in

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patients who developed generalized tonic-clonic seizures (GTCS) and in those with the longest follow-up. In long-term follow-up of absence epilepsy (AE) patients, the incidence of GTCS was 50%. Of those with AE and GTCS, 35% were seizure free, whereas in the 50% with AE uncomplicated by GTCS, 78% were seizure free.

DRUG-INDUCED EXACERBATION OF BECTS

The incidence of drug-induced exacerbation of benign epilepsy with centrotemporal spikes (BECTS) was determined retrospectively in 82 patients examined at the Centre Saint Paul, Marseille, France. Among 40 patients treated with carbamazepine (35 monotherapy, 5 polytherapy) 1 showed electroclinical exacerbation that was dose related; discontinuation of CBZ was followed by immediate improvement. Among 14 taking phenobarbital (9 monotherapy, 5 polytherapy), 1 treated with CBZ and PB showed EEG exacerbation; the EEG improved after withdrawal of the PB while continuing CBZ. In 45 patients exposed to valproate (VPA) and 8 receiving benzodiazepine (BZP), none showed exacerbation. A spontaneous worsening of BECTS facilitated by the AED was considered a possibility. (Corda D, Gelisse P, Genton P et al. Incidence of drug-induced aggravation in benign epilepsy with centrotemporal spikes. Epilepsia June 2001;42:754-759). (Reprints: Dr Pierre Genton, Centre Saint Paul, 13258 Marseille 09, France).

COMMENT. These authors found a minor risk of AED-exacerbation of BECTS. CBZ and phenobarbital were involved in only one case each, whereas VPA and BZP-treated patients showed no aggravation. Two previous reports of CBZ-exacerbation of BECTS are cited (Lerman, 1986; Caraballo et al, 1989).

An exacerbation of seizures and partial status epilepticus in 6 young, mentally retarded adults treated with CBZ polytherapy was related to excessive levels of CBZ-10, 11-epoxide, in a report from the Marshfield Clinic WI, and Mayo Clinic, MN. (So EL et al, 1994; see Progress in Pediatric Neurology III, 1997;pp142-143). CBZ-epoxide serum levels are important in CBZ-treated patients with seizure exacerbation.

Neuropsychological dysfunction and BECTS. Interictal epileptic discharges (IED) during sleep in patients with BECTS may be associated with impaired neuropsychological function. After spontaneous remission of the IED in 5 of 9 patients followed for 2 years, re-evaluation showed an increase in IQ scores and improvement in visuomotor coordination, memory, and attention. (Baglietto MG et al. Dev Med Child Neurol June 2001;43:407-412). The authors adocate further trials of high dose diazepam in short cycles to block interictal epileptic discharges in sleep in these patients.

KETOGENIC DIET IN INFANTS WITH REFRACTORY EPILEPSY

The effectiveness, tolerability, and adverse effects of the ketogenic diet were reviewed retrospectively in 31 infants (18 male; 13 female) with refractory epilepsy treated at Columbia-Presbyterian Medical Center, New York, NY. A 3:1 or 4:1 (fat:nonfat) ketogenic regimen was introduced slowly after a 12-38 hour in-patient fasting period to initiate ketosis. The ratio of the diet was adjusted to produce moderate to strong ketosis. Adequate calories and protein to sustain growth were provided. Mean age at start of diet was 13.8+/-5.7 months; 14 were <12 months and 17 >12 months. The duration on the diet was <3 months in 3, 3-5 mo in 7, and =/>6 mo in 21 (67%). Epilepsy etiology was idiopathic in 12(39%) and symptomatic in 19(61%); 4 patients had progressive metabolic and degenerative